

1. A method for identifying a compound that inhibits transmission of HIV to a target cell, the method comprising contacting synthetic peptide comprising trimers in the presence of a compound and with HR2 peptide under conditions and for a time sufficient to allow formation of a complex between the synthetic peptide comprising trimers and HR2 peptide *in vitro*; and detecting the amount of complex formed; wherein inhibition or reduction of complex formation in the presence of the compound, as compared to complex formation in the absence of the compound, is indicative of ability of the compound to inhibit transmission of HIV to a target cell; and

wherein synthetic peptide comprises an amino acid sequence derived from the HR1 region of HIV-1 gp41; wherein the HR1 region consists of native amino acid sequence shown as SEQ ID NO:1 or polymorphisms thereof; wherein the HR1 region from which the synthetic peptide is derived comprises a hydrophobic domain of amino acids corresponding to amino acid residues in positions 28 to 36 of SEQ ID NO:1 or polymorphisms thereof; wherein the amino acid residues comprising the hydrophobic domain correspond to heptad repeat positions "efgabcdef"; and wherein the amino acid sequence of the synthetic peptide further comprises one or more amino acid substitutions in the heptad repeat positions "efgabcdef" comprising the hydrophobic domain, as compared to the native amino acid sequence of the HR1 region, which enables synthetic peptide to self-assemble in solution into trimers.

2. The method according to claim 1, wherein the amino acid sequence of the synthetic peptide comprises one or more amino acid substitutions in the hydrophobic domain comprising either a substitution in the "c" position, or a substitution in both the "g" position and the "c" position, of the heptad repeat positions "efgabcdef".

3. The method according to claim 2, wherein the synthetic peptide comprises an amino acid substitution additional to a substitution in either the "c" position or both the "g" position and "c" position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of an "a" position, a "d" position, a "b" position, and a combination thereof.

4. The method according to claim 1, wherein the amino acid sequence of the synthetic peptide comprises one or more amino acid substitutions in the hydrophobic

domain comprising the heptad repeat positions "efgabcdef" that are in a position of the heptad repeat positions selected from the group consisting of a C-terminal "e" position, a C-terminal "f" position, and a combination thereof.

5. The method according to claim 4, wherein the synthetic peptide comprises an amino acid substitution additional to the substitution in one or more of the "e" position and the "f" position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of the "a" position, a "d" position, a "b" position, and a combination thereof.

6. The method according to claim 1, wherein the synthetic peptide further comprises a component selected from the group consisting of one or more reactive functionalities, a macromolecular carrier, a pharmaceutically acceptable carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide, and a combination thereof.

7. The method according to claim 1, wherein the synthetic peptide is predominately in trimeric form.

8. The method according to claim 1, wherein the synthetic peptide is in a monomer-trimer equilibrium.

9. A method for producing a drug that inhibits transmission of HIV to a target cell, the method comprising contacting synthetic peptide comprising trimers in the presence of a compound and with HR2 peptide under conditions and for a time sufficient to allow formation of a complex between the synthetic peptide comprising trimers and HR2 peptide *in vitro*; and detecting the amount of complex formed; wherein inhibition or reduction of complex formation in the presence of the compound is indicative of ability of the compound to inhibit transmission of HIV to a target cell; and wherein the drug comprises the compound contacted with a pharmaceutically acceptable carrier in producing the drug; and wherein synthetic peptide comprises an amino acid sequence derived from the HR1

region of HIV-1 gp41; wherein the HR1 region consists of native amino acid sequence shown as SEQ ID NO:1 or polymorphisms thereof; wherein the HR1 region from which the synthetic peptide is derived comprises a hydrophobic domain of amino acids corresponding to amino acid residues in positions 28 to 36 of SEQ ID NO:1 or polymorphisms thereof; wherein the amino acid residues comprising the hydrophobic domain correspond to heptad repeat positions "efgabcdef"; and wherein the amino acid sequence of the synthetic peptide further comprises one or more amino acid substitutions in the heptad repeat positions "efgabcdef" comprising the hydrophobic domain, as compared to the native amino acid sequence of the HR1 region, which enables synthetic peptide to self-assemble in solution into trimers.

10. The method according to claim 9, wherein the amino acid sequence of the synthetic peptide comprises one or more amino acid substitutions in the hydrophobic domain comprising either a substitution in the "c" position, or a substitution in both the "g" position and the "c" position, of the heptad repeat positions "efgabcdef".

11. The method according to claim 10, wherein the synthetic peptide comprises an amino acid substitution additional to a substitution in either the "c" position or both the "g" position and "c" position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of an "a" position, a "d" position, a "b" position, and a combination thereof.

12. The method according to claim 9, wherein the amino acid sequence of the synthetic peptide comprises one or more amino acid substitutions in the hydrophobic domain comprising the heptad repeat positions "efgabcdef" that are in a position of the heptad repeat positions selected from the group consisting of a C-terminal "e" position, a C-terminal "f" position, and a combination thereof.

13. The method according to claim 12, wherein the synthetic peptide comprises an amino acid substitution additional to the substitution in one or more of the "e" position and the "f" position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of the "a"

position, a “d” position, a “b” position, and a combination thereof.

14. The method according to claim 9, wherein the synthetic peptide further comprising a component selected from the group consisting of one or more reactive functionalities, a macromolecular carrier, a pharmaceutically acceptable carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide, and a combination thereof.

15. The method according to claim 9, wherein the synthetic peptide is predominately in trimeric form.

16. The method according to claim 9, wherein the synthetic peptide is in a monomer-trimer equilibrium.

17. In a method for identifying or producing a molecule that can inhibit the binding between HR1 and HR2 regions of HIV gp41, the improvement which comprises: use of a trimer as a binding partner with HR2 peptide in detecting *in vitro* the ability of the molecule to bind to an HR (heptad repeat) region of HIV gp41;

wherein the trimer is comprised of synthetic peptide comprising an amino acid sequence derived from the HR1 region of HIV-1 gp41; wherein the HR1 region consists of native amino acid sequence shown as SEQ ID NO:1 or polymorphisms thereof; wherein the HR1 region from which the synthetic peptide is derived comprises a hydrophobic domain of amino acids corresponding to amino acid residues in positions 28 to 36 of SEQ ID NO:1 or polymorphisms thereof; wherein the amino acid residues comprising the hydrophobic domain correspond to heptad repeat positions “efgabcdef”; and wherein the amino acid sequence of the synthetic peptide further comprises one or more amino acid substitutions in the heptad repeat positions “efgabcdef” comprising the hydrophobic domain, as compared to the native amino acid sequence of the HR1 region, which enables synthetic peptide to self-assemble in solution into trimers.

18. The method according to claim 17, wherein the amino acid sequence of the synthetic peptide comprises one or more amino acid substitutions in the hydrophobic domain comprising either a substitution in the “c” position, or a substitution in both the

“g” position and the “c” position, of the heptad repeat positions “efgabcdef”.

19. The method according to claim 18, wherein the synthetic peptide comprises an amino acid substitution additional to a substitution in either the “c” position or both the “g” position and “c” position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of an “a” position, a “d” position, a “b” position, and a combination thereof.

20. The method according to claim 17, wherein the amino acid sequence of the synthetic peptide comprises one or more amino acid substitutions in the hydrophobic domain comprising the heptad repeat positions “efgabcdef” that are in a position of the heptad repeat positions selected from the group consisting of a C-terminal “e” position, a C-terminal “f” position, and a combination thereof.

21. The method according to claim 20, wherein the synthetic peptide comprises an amino acid substitution additional to the substitution in one or more of the “e” position and the “f” position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of the “a” position, a “d” position, a “b” position, and a combination thereof.

22. The method according to claim 17, wherein the synthetic peptide further comprising a component selected from the group consisting of one or more reactive functionalities, a macromolecular carrier, a pharmaceutically acceptable carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide, and a combination thereof.